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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/945,505	08/31/2001	Alison E. Anastasio	MWH-30US	3529

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NEW HAVEN, CT 06511

EXAMINER

GOLDBERG, JEANINE ANNE

ART UNIT PAPER NUMBER

1634

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/945,505	ANASTASIO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 15 May 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 13-21, 24, 25, 28 and 34-39 is/are pending in the application.
- 4a) Of the above claim(s) 36-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13-20, 24 and 28 is/are rejected.
- 7) ☒ Claim(s) 21, 25, 34 and 35 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                      | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u>0801</u> . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                             | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)                   |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>11/01</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. This action is in response to the papers filed May 15, 2003. Currently, claims 13-21, 24-25, 28, 34-39 are pending. Claims 36-39 have been withdrawn as drawn to non-elected subject matter.

### ***Election/Restrictions***

2. Applicant's election of Group VI (Claims 13-21, 24-25, 28, 34-35) in the paper filed May 15, 2003 is acknowledged.

Upon further consideration, the examiner would like to clarify the restriction requirement for the pending claims. Claims 13-19, 24 link(s) inventions drawn to each of the independent and distinct isogenes (namely 27 isogenes). The restriction requirement between linked inventions is subject to the nonallowance of the linking claim(s), claims 13-19. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

As noted in the Interview of July 8, 2003, the examiner has agreed to rejoin the isogene nucleic acids with the genome anthology comprising the selected isogene. The response clarifies the structure of the genome anthologies to be directed to a collection of isogenes. Thus, the examiner will examine the combination of isogenes which includes isogene 2. As provided in 803.04 of the MPEP, based upon the finding of allowable sequences, claims limited to the allowable sequences, all combinations containing the allowable sequences and any patentably indistinct sequences will be rejoined and allowed. "Rejoinder will be permitted for claims requiring any allowable sequence(s). Any claims which have been restricted and nonselected and which are limited to the allowable sequence(s) will be rejoined and examined."

The response further traverses the restriction requirement directed to restriction to a single isogene (see page 12 of Response filed May 15, 2003). The response states that Claim 20 is directed to a genus of TNFRSF1A isogene sequences that encode a TNFRSF1A polypeptide with a domain capable of binding TNFalpha. First, the response argues that a restriction requirement may not be applied to a Markush claim. This argument has been thoroughly reviewed, but is not found persuasive because each isogene is a patentably distinct invention. As provided in the MPEP, "The term "distinct" means that two or more subjects as disclosed are related, for example, as combination and part (subcombination) thereof, process and apparatus for its practice, process and product made, etc., but are capable of separate manufacture, use, or sale as claimed, AND ARE PATENTABLE (novel and unobvious) OVER EACH OTHER (though they may each be unpatentable because of the prior art)." Under the

statute an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent (MPEP § 806.04 - § 806.04(i)) or distinct (MPEP § 806.05 - § 806.05(i)). The instant isogenes are not obvious over one another. For example, given isogene 1, it is not obvious to obtain isogene 2 with a different nucleic acid structure with different combinations of polymorphisms. The instant specification states that although polymorphic sites were reported previously, nothing in that reference discloses or suggests the existence of polymorphic sites. This clearly implies that the specification believes that various combinations of polymorphisms are distinct. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Since the linking claims have not been deemed allowable for the reasons set forth below, the restriction limiting the examination to isogene 2, as selected by applicants is maintained.

Applicant's argues that the claims must be examined over the entire Markush group because "unity of invention in a Markush group exists when its members "(1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility." The disclosed utilities in the instant specification related to the

differences in nucleotide structure and amino acid structure. For example, the haplotyping method, the screening for compounds method, the association of traits and haplotype claims are all directed to the differences between the haplotypes in nucleic acid structure. All of the disclosed utilities go to the differences found between the isogene sequences. Moreover the substantial structural feature disclosed as being essential to these utilities found in the specification are not common between the isogenes. As discussed above, the different combinations of polymorphisms which are used to generate the isogenes is not shared. Therefore, the Markush-type claim of Claim 20 lacks unity of invention as set forth in MPEP 803.02. The utility asserted in the instant response of "encoding a TNFRSF1A polypeptide with a domain capable of binding TNFalpha" does not appear in the originally filed specification. Therefore, at the time the invention was made, it does not appear that applicants contemplated such a "utility."

3. Claims 36-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

4. The requirement is still deemed proper and is therefore made FINAL. This application contains subject matter drawn to an invention nonelected with traverse in the paper filed May 15, 2003. The subject matter directed to isogenes. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

***Claim Rejections - 35 USC § 112-Description***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 24, 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 24 and 28 are drawn to nucleic acids minimally containing 15 nucleotides from SEQ ID NO: 1 or SEQ ID NO: 2.

The claims broadly encompass nucleic acid fragments, cDNA, and genomic nucleic acids which minimally comprise 15 nucleotides from the recited positions, namely, PS1, PS4, PS12, PS14, PS15, PS17 and PS18 of SEQ ID NO: 1 and nucleotides 224, 362, 403, and 935 of SEQ ID NO: 2. The claim requires a partial structure of 15 nucleotides from SEQ ID NO: 1 or 2. The claim therefore broadly encompasses additional variants, splice variants, mutations, homologues, sequences from additional species.

*Vas-Cath Inc. V. Mahurkar*, 19 USPQ2b 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed”. Applicant is reminded that *Vas-*

*Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, Applicant has defined only a fragment of a nucleic acid sequence. The claims read on TNFRSF1A variants, splice variants, mutations, homologues, sequences from additional species. For example, the post filing date art teaches additional mutations and variations within the TNFRSF1A gene which cause associated periodic syndrome. Specifically, Aganna ( Arthritis & Rheumatism, Vol.. 46, No. 1, page 245-249, January 2002) teaches a transition encoding a Cys70Arg variant in exon 3. The instant specification does not teach a variation in exon 3 changing the coding sequence from C70R. Moreover, Aganna et al (Eur. J. Human Genetics, Vol. 9, pages 63-66, 2001) teaches a mutation in the TNFRSF1A gene which reduced plasma



TNFRSF1A levels at R92P. The instant specification fails to teach a mutation of R92P. Aksentijevich et al (Am. J. Hum. Genet. Vol. 69, pages 301-314, 2001) teaches four novel mutations in the TNFRSF1A gene and a splice-acceptor site upstream of exon 3 (abstract). As seen in Figure 3, an aberrantly spliced transcript begins prior to exon 3, thus generating a variant cDNA and protein sequence. The instant specification does not contemplate or teach aberrantly spliced transcripts. Therefore, based upon the post-filing date art, the instant claims encompass a large number embodiments within the scope of the claim which have not been described. The knowledge in the art concerning alleles does not provide any indication of how the structure of one allele is representative of unknown alleles. The nature of alleles is that they are variant structures, and in the present state of the art the structure of one does not provide guidance to the structure of others. The common attributes of the genus are not described. One of skill in the art would conclude that applicant was not in possession of the claimed genus because the description of the isogenes is not representative of the genus and is insufficient to support the claim.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 13-14, 16, 20, 28 are rejected under 35 U.S.C. 102(a) as being anticipated by Nandabalan et al (WO 00/50436, August 2000).

It is noted that the inventorship of WO 00/50436 and the instant application are different.

Nandabalan et al. (herein referred to as Nandabalan) teaches polymorphisms and haplotypes within the TNFRSF1A gene (also referred to as TNFR1 gene). Nandabalan teaches PCR primer pairs located in various regions of the gene. SEQ ID NO: 78 is upstream of PS4, PS12, PS14, PS15, PS17 and PS18. Thus, SEQ ID NO: 78 of Nandabalan is an isolated oligonucleotide which may be used to amplify the gene and used to detect polymorphisms at positions PS4, PS12, PS14, PS15, PS17 and PS18 (limitations of Claim 13). The primer of Nandabalan specifically hybridizes to an allele of the TNFRSF1A gene at a region containing the polymorphic site. For example, the primer hybridizes to the region upstream of exon 1 where PS4 is located, therefore, the primer hybridizes to the same region (limitations of Claim 14). The oligonucleotide is consider a primer, therefore, nucleic acid is a primer extension oligonucleotides (limitations of Claim 16).

Claim 20 is directed to a nucleic acid comprising a nucleotide sequence which is complementary to a nucleotide sequence comprising nucleotides 2920-4210, 11417-

12926 and 14634-16768 of SEQ ID NO: 43. The specification appears to make a distinction between a nucleotide sequence which is complementary to a nucleotide sequence and a nucleotide sequence which is a "perfect" or "complete" complement (page 13, lines 7-22). Nandabalan teaches SEQ ID NO: 79 which is complementary to position 3516-3536 of SEQ ID NO: 2 of the instant application (limitations of Claim 20b).

With respect to Claim 28, as explained by the instant specification, PS2, PS3, PS5-PS11, PS13 and PS16 were described in Table 3 of WO 00/50436 (page 4, lines 15-20). Nandabalan teaches ASO probes and primers for each of these polymorphic sites. For example, SEQ ID NO: 39 of Nandabalan comprises 15 nucleotides comprising a T at position 224 of SEQ ID NO: 2 (page 19)(limitations of Claim 28). Similarly, Nandabalan teaches 15-mers comprising an A at position 362 and a C at position 403 of SEQ IDNO: 2. Additionally, Nandabalan teaches allele-specific oligonucleotide probes which comprise at least 15 nucleotides (page 19). SEQ ID NO: 15 of Nandabalan comprises 15 contiguous nucleotides from SEQ ID NO: 2 of the instant application including a T at position 224 of SEQ ID NO: 2. Thus, Nandabalan anticipates the claimed invention.

7. Claims 13-14, 16, 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5,474,796, December 12, 1995).

Brennan teaches oligonucleotides having 10 nucleotides each (10-mers). The oligonucleotides represent every possible permutation of the 10-mer oligonucleotide. Therefore, Brennan teaches every possible 10-mer nucleic acid.

Claim 13 is drawn to an isolated oligonucleotide designed to detect a polymorphism. Since Brennan teaches every possible 10-mer oligonucleotide, Brennan teaches an array of different nucleotides which would achieve the function of detecting a polymorphism. The claims does not provide any length limitation or other structural features.

Claim 14 is directed to an oligonucleotide which is allele specific and hybridizes to a region containing the polymorphism. The genus of oligonucleotides which is encompassed by the claim significantly overlaps the genus of Brennan.

Claim 16 is directed to primers which are primer-extension oligonucleotides. Since Brennan teaches each ten-mer oligonucleotide without a blocked nucleotide, the oligonucleotides of Brennan may be used as primer-extension oligonucleotides.

Claim 20 is directed to an isolated polynucleotide which is complementary to a nucleotide sequence comprising 2920-4210, 11417-12926 and 14634-16768 of SEQ ID NO: 43. The specification appears to make a distinction between a nucleotide sequence which is complementary to a nucleotide sequence and a nucleotide sequence which is a "perfect" or "complete" complement (page 13, lines 7-22). Thus, the 10-mer nucleic acids would be complementary to the claimed nucleic acids. Ten-mer nucleic acids would be complementary to the nucleotide sequences claimed.

Therefore because Brennan teaches every element of the claims, Brennan anticipates the claimed invention.

8. Claims 13-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Hauptmann et al. (Genbank Accession Number A29098, July 1995).

Hauptmann et al. (herein referred to as Hauptmann) teaches a nucleic acid for TNF-receptor. The nucleic acid of Hauptmann is an oligonucleotide which can detect a polymorphism at PS 17 and is allele-specific (limitations of Claim 14). The nucleic acid of Hauptmann contains SEQ ID NO: 9 (limitations of Claim 15). Moreover, the nucleic acid of Hauptmann is extendable (limitations of Claim 16) and comprises SEQ ID NO: 35, for example (limitation of Claim 17). The nucleic acid of Hauptmann is extendable because the final nucleotide is not a blocking nucleotide. Thus, the nucleic acid is capable of primer extension. Therefore because Hauptmann teaches every element of the claims, Hauptmann anticipates the claimed invention.

9. Claims 13-14, 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Prashad et al. (WO 94/02500, February 3, 1994).

Prashad teaches a nucleic acid oligonucleotide for detecting chromosomal translocations. The oligonucleotide comprises SEQ ID NO: 27 (limitations of Claim 17). The oligonucleotide specifically hybridizes to an alleles of the TNFRSF1A gene at a region containing the polymorphic site. The nucleic acid of Prashad would hybridize to a region, namely upstream of exon 1 (limitations of Claim 14). SEQ ID NO: 47 of Prashad is a primer extension oligonucleotides comprising SE QID NO: 27 (limitations of Claim 16-17). Therefore because Prashad teaches every element of the claims, Prashad anticipates the claimed invention.

10. Claims 13-14, 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Brewer et al (WO 97/31011, August 1997).

Brewer et al. (herein referred to as Brewer) teaches a nucleic acid oligonucleotide which comprises SEQ ID NO: 26. The nucleic acid is an oligonucleotide which is capable of an extension reaction (limitations of Claims 16-17). The nucleic acid of Brewer would hybridize to a region, namely upstream of exon 1 (limitations of Claim 14). Therefore because Brewer teaches every element of the claims, Brewer anticipates the claimed invention.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brennan (US Patent 5,474,796, December 12, 1995) in view of Ahern ( The Scientist, Vol 9, No. 15, page 20, July 1995).

Brennan teaches oligonucleotides having 10 nucleotides each (10-mers). The oligonucleotides represent every possible permutation of the 10-mer oligonucleotide. Therefore, Brennan teaches every possible 10-mer nucleic acid. Claim 13 is drawn to an isolated oligonucleotide designed to detect a polymorphism. Since Brennan teaches every possible 10-mer oligonucleotide, Brennan teaches an array of different nucleotides which would achieve the function of detecting a polymorphism. The claims does not provide any length limitation or other structural features. Claim 14 is directed to an oligonucleotide which is allele specific and hybridizes to a region containing the polymorphism. The genus of oligonucleotides which is encompassed by the claim significantly overlaps the genus of Brennan. Claims 16 and 17 are directed to primers which comprise a nucleotide sequence of 10 nucleotides, namely SEQ ID NO: 25-38. Brennan teaches each of these oligonucleotides.


Brennan does not specifically teaches packaging necessary reagents into a kit.

However, Ahern teaches reagent kits offer scientists good return on investment. Ahern teaches kits save time and money because the kits already comes prepared.

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have modified the teachings of Brennan with the teachings of Ahern to incorporate the necessary reagents into a packaged kit. The ordinary artisan would have been motivated to have packaged the primers, probes, and

reagents of Brennan into a kit, as taught by Ahern for the express purpose of saving time and money.

***Allowable Subject Matter***

13. The prior art does not teach a nucleic acid comprising nucleotides 2920-4210, 11417-12926 and 14634-16768 of SEQ ID NO: 43. Moreover, any combination of isogene nucleic acids comprising the nucleic acid would be free of the art. 

14. Claims 21, 35 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

15. Claims 21, 25, 34, 35 are objected to as containing non-elected subject matter.

***Conclusion***

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) Anastasio et al. (US Pat. 6,521,747 B2, February 18, 2003) is directed to isogenes from the AGTR1 gene.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

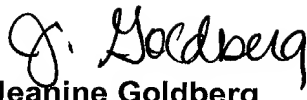
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.



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**Jeanine Goldberg**  
**Patent Examiner**  
August 25, 2003